[0067] Another method of establishing percent identity in the context of the present invention is to use the MPSRCH package of programs copyrighted by the University of Edinburgh, developed by John F. Collins and Shane S. Sturrok, and distributed by IntelliGenetics, Inc. (Mountain View, Calif.). From this suite of packages the Smith-Waterman algorithm can be employed where default parameters are used for the scoring table (for example, gap open penalty of 12, gap extension penalty of one, and a gap of six). From the data generated the Match value reflects sequence identity. Other suitable programs for calculating the percent identity or similarity between sequences are generally known in the art, for example, another alignment program is BLAST, used with default parameters. For example, BLASTN and BLASTP can be used using the following default parameters: genetic code=standard; filter=none; strand=both; cutoff=60; expect=10; Matrix=BLOSUM62; Descriptions=50 sequences; sort by=HIGH SCORE; Databases=non-redundant, GenBank +EMBL +DDBJ +PDB +GenBank CDS translations-FSwiss protein+Spupdate+PIR.

[0068] Alternatively, homology can be determined by hybridization of polynucleotides under conditions which form stable duplexes between homologous regions, followed by digestion with single-stranded-specific nuclease(s), and size determination of the digested fragments. DNA sequences that are substantially homologous can be identified in a Southern hybridization experiment under, for example, stringent conditions, as defined for that particular system. Defining appropriate hybridization conditions is within the skill of the art. See, e.g., Sambrook et al., supra; DNA Cloning, supra; Nucleic Acid Hybridization, supra.

[0069] Systems for cloning and expression of a polypeptide in a variety of different host cells are well known. Suitable host cells include bacteria, mammalian cells, yeast and baculovirus systems. Mammalian cell lines available in the art for expression of a heterologous polypeptide include Chinese hamster ovary cells, COS cells, HeLa cells, baby hamster kidney cells and many others. A common, preferred bacterial host is *E. coli*.

[0070] Suitable vectors can be chosen or constructed, containing appropriate regulatory sequences, including promoter sequences, terminator fragments, polyadenylation sequences, enhancer sequences, marker genes and other sequences as appropriate. For further details see, for example, Molecular Cloning: a Laboratory Manual: (Sambrook and Russell 2001), or Short Protocols in Molecular Biology, eds. (Ausubel 2002). Transformation procedures depend on the host used, but are well known.

[0071] Nucleic acid for use according to the invention may be DNA or RNA, and may be single-stranded or double-stranded, cDNA, genomic DNA or wholly or partially synthetic. Double-stranded DNA is preferred.

[0072] A wide variety of bifunctional or polyfunctional cross-linking reagents, both homo- and heterofunctional, are known in the art and are commercially available (e.g. Pierce Chemical Co., Rockford, Ill.). Such cross-linking reagents may be reacted with the antigen and ligand by standard methods (e.g. according to the manufacturers instructions). Following cross-linkage, the antigen-ligand complex may be purified from unreacted antigen and ligand by standard methods (e.g., chromatography, SDS-PAGE and the like). The efficacy of chemically cross-linked compositions in stimulating intracellular signals in B cells (e.g. increased intracellular calcium concentrations) and/or modulating immune responses can be evaluated using assays, e.g. as described herein.

[0073] The administration of a recombinant vaccine may be for a prophylactic purpose (vaccination, e.g. anti-microbial) or therapeutic, e.g. in immunotherapy (e.g. anti-microbial or anti-tumour). Vaccination may be used to confer on a subject protective immunity to an antigen.

[0074] In accordance with the present invention antibody production in vitro, e.g. in culture, may be stimulated. For example, B cells specific for an antigen of interest may be cultured with a stimulatory composition of the invention to stimulate production by the B cells of antibody for the antigen of interest. The antibodies produced may be isolated from the culture medium, e.g. by virtue of their binding capability for the antigen.

[0075] In a further aspect, the present invention provides a pharmaceutical composition which comprises a CeLTOS antigen/immunogen as disclosed.

[0076] Pharmaceutical compositions according to the present invention may comprise, in addition to the antigen/immunogen, a pharmaceutically acceptable excipient, carrier, vehicle, buffer, stabiliser or other materials well known to those skilled in the art. Such materials should be non-toxic and should not interfere with the efficacy of the active ingredient. The precise nature of the carrier or other material will depend on the route of administration, which will preferably be cutaneous, subcutaneous or intravenous injection, especially subcutaneous.

[0077] For parental, intravenous, cutaneous or subcutaneous injection, the active ingredient will be in the form of a parenterally acceptable aqueous solution which is pyrogen-free and has suitable pH, isotonicity and stability. Those of relevant skill in the art are well able to prepare suitable solutions using, for example, isotonic vehicles such as Sodium Chloride Injection, Ringer's Injection, Lactated Ringer's Injection. Preservatives, stabilisers, buffers, antioxidants and/or other additives may be included, as required. Sub-cutaneous injection may be preferred route of administration.

[0078] A pharmaceutical composition in accordance with the present invention may comprise one or more additional active ingredients. For example, the composition may contain an additional agent that has immunomodulatory properties, such as a cytokine or (additional) adjuvant.

[0079] Antibodies which are specific for a target of interest may be obtained using techniques which are standard in the art. Methods of producing antibodies include immunising a mammal (eg mouse, rat, rabbit, horse, goat, sheep or monkey) with the protein or a fragment thereof, or a cell or virus which expresses the protein or fragment. Immunisation with DNA encoding a target polypeptide is also possible. Antibodies may be obtained from immunised animals using any of a variety of techniques known in the art, and screened, preferably using binding of antibody to antigen of interest. For instance, Western blotting techniques or immunoprecipitation may be used (Armitage, Fanslow et al. 1992).

[0080] As an alternative or supplement to immunizing a mammal, an antibody may be obtained from a recombinantly produced library of expressed immunoglobulin variable domains, eg using lambda bacteriophage or filamentous bacteriophage which display functional immunoglobulin binding domains on their surfaces; for instance see WO92/01047. The library may be naive, that is constructed from sequences obtained from an organism which has not been immunized